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Short Review

Candidiasis in Birds: An Update

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ABSTRACT

Candidiasis is a fungal disease that is induced by yeast from the genus *Candida* spp. This opportunistic pathogen is present in the skin and gastrointestinal tract of the host, and it tends to induce disease when the host's immune system is suppressed. The aim of this study was to present a short review of Candidiasis in birds, covering aspects, such as host, species, pathogeny, and diagnosis. Candida comprises approximately 200 species, but only a few of them are pathogenic. Among these, *Candida albicans* is the most frequently isolated in clinical cases. *Candida* spp. is a polymorphic fungus that can appear in the form of budding yeast, hyphae, or *pseudohyphae,* depending on the growth environment. They are pretty common in birds, being observed in almost every species. In birds, they can cause infections in the upper digestive system and skin. Clinically, candidiasis in birds is characterized by low morbidity and mortality rates. Affected birds typically display nonspecific indications like depression, anorexia, and inhibited growth. Diagnosis can be performed by laboratory culture, cytology, histopathology, and PCR. On postmortem examination is possible to observe a pseudomembrane with a whitish to yellowish color, easily removed, and an eroded mucosal epithelium of the crop. Infections can be prevented by good sanitary conditions.

1. Introduction

Candidiasis is a sporadic fungal disease caused by yeast belonging to the genus *Candida*[1,2]. Healthy animals are carriers of diverse species of *Candida* in their normal flora[3]. Candidiasis usually occurs when the immune system of the animals is compromised and can be either primary or secondary[4]. It can affect the respiratory tract, central nervous system, digestive tract, skin, and other organs. This disease has been isolated from diverse species of vertebrates, particularly birds (both domestic and wild)[4,5]. This short review aimed to describe the main yeast species, host, epidemiology, pathogeny, diagnosis, and treatments of Candidiasis in birds.

2. Pathogeny

2.1. Species of Candida and hosts

There are about 200 species of *Candida*, but only a few of them are pathogenic[3–5]. These species of yeast have been isolated from plants and animals worldwide. In animals, *Candida* spp. are regarded as commensals and can be found in the skin, digestive, and urogenital systems of healthy individuals. *Candida albicans* is the most common species isolated from clinical cases from animals and humans. Other isolates of *Candida* include *C. salmonicola, C. guilliermondii, C. ravautii, C. parapsilosis, C. catenulata, C. famata, C. brumptii, C. rugosa,* and *C. tropicalis* [3,5]. The hosts of *Candida* include a large variety of bird species, including domestic poultry, waterfowls, and wild birds[5,6]. Table 1 shows some examples of host and isolated species of *Candida* spp.

2.2. Predisposed factors to occur infection

Candida is an opportunistic pathogen. When the immune system of the animal is compromised, this yeast can grow and cause clinical disease[16]. Other predisposing factors include immunosuppressive conditions (for example, malnutrition, debilitation), concurrent disease, parasitism (coccidiosis), overpopulation, young birds that

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Table 1. Examples of bird species and isolated *Candida* species

Avian species	*Candida* (*C.*) species	Reference
Amazona spp.	*C. humicola, C. parapsilosis, C. guilliermondii, C. famata, C. albicans.*	7
Columbia livia	*C. parapsilosis complex, C. tropicalis, C. krusei, C. Glabrata, C. rugosa*	8
Gallus domesticus	*Candida albicans, C. tropicalis, C.glabrata, C. lusitanie and C. guilliermondii*	9,10
Amazona auropalliata	*C. glabrata*	11
Streptopelia capicola	*C. glabrata*	11
Ara ararauna	*C. glabrata*	11
Nymphicus hollandicus	*C. glabrata*	11
Pionus senilis	*C. krusei*	11
Struthio camelus	*C. albicans*	12
Branta canadensis	*C. albicans*	13
Gyps fulvus	*C. albicans, C. parapsilosis*	14
Accipiter nisus	*C. albicans, C. zeylanoides*	14
Accipiter gentilis	*C. albicans*	14
Falco tinnunculus	*C. albicans, C. parapsilosis,*	14
Athena noctua	*C. albicans*	14
Milvus milvus	*C. lusitanea*	15

are not fully immunocompetent (less than 3 months), long-term use of antimicrobial therapy, poor hygiene in the environment and food preparation, poor hygiene of the animal, hypovitaminosis A, aflatoxicosis, high concentrations of sugar in fruit, contaminated formulas, alkaline crop, and forced hand-rearing[2,17].

2.3. Source and root of transmission

Since *Candida* is part of the normal flora of birds, the sources of infections are primarily endogenous[6]. Exogenous sources of contamination can occur when a non-infected bird has direct contact with an infected bird, contaminated secretions, feces, or water by ingestion [5,6,17](Figure 1). Candidiasis can also be transmitted through contaminated water recirculation systems in the domestic animals' industry. *Candida* spp. can survive cleaning processes such as chlorination, ultra violate light, filtration, and turbidity [6].

2.4. Pathogenic characteristic of Candida spp.

Candida spp. has virulence factors, such as integrin-like molecules, proteases, and phospholipases that help them to attach to and invade host tissues, producing disease[17].

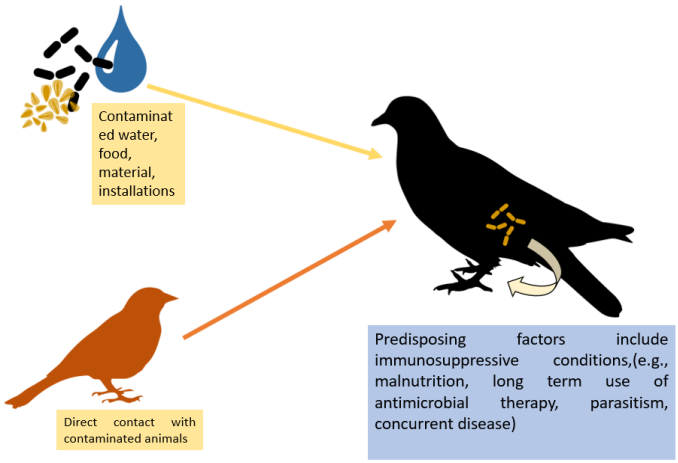

Figure 1. Exogenous and endogenous sources of *Candida* spp. contamination (Source: Andreia Garcês).

Other factors that help in the evasion of the animal's immune mechanisms are biofilm formation and phenotypic switching[13]. In an immune-compromised bird, the yeasts can attach themselves to the mucosal cells and rapidly change their form from yeast to hyphal form, which the phagocytic cannot eliminate[18].

3. Clinical signs

Initial clinical signs of Candidiasis in birds are nonspecific. The most common form is enteric infection (crop is the most affected organ, but the oral cavity, proventriculus, and ventriculus also can be affected)[5]. Cutaneous candidiasis and comb candidiasis can also be observed, leading to feather loss and significant morbidity[5]. In adults, it is possible to observe lethargy, anorexia, ruffled feathers, and stunting. In younger birds, where the disease usually is more severe, it is possible to observe anorexia, lethargy, crop stasis, delayed crop emptying, regurgitation, and white plaques in the oral cavity[6,10]. When the birds develop infections in the oral cavity, they can present difficulty in swelling, halitosis, regurgitation, diarrhea, depression, whitish plaques in the oral cavity (Figure 2), and crop stasis[5,6]. In more severe instances, advanced cases of candidiasis can lead to observable changes in the affected bird. These alterations may include a thickened crop, which is sometimes referred to as a "Turkish-towel" appearance due to its

Figure 2. Whitish plaques in the oral cavity of birds compatible with Candidiasis (orange arrow; A -*Merops apiaster*, B- *Buteo buteo;* Source: Andreia Garcês).

texture resembling that of a towel, as well as a swollen or mucus-filled crop. Additionally, beak abnormalities may manifest in birds afflicted with candidiasis.[18].

3.1. Post-mortem

During the post-mortem, it is possible to observe the formation of yellowish to whitish pseudomembranes that are easy to peel, and the mucus membrane under these diphtheritic materials is usually eroded. These lesions can be observed in the crop, oropharynx, and proximal esophagus [6,18]. Post-mortem tissue or biopsy samples can be collected and stained with Periodic Acid-Schiff or Gomorimethylamine silver[5]. *Candida* spp. usually takes the form of hyphae that can be observed under microscopy, with hyphae growing perpendicular to the surface of the mucosa[6]. It is also possible to observe pseudohyphae and budding yeast forms, especially in the sloughed epithelium [5,16]. *Candida* spp. hyphae start to penetrate the stratum corneum and the upper parts of the stratum spinosum of the stratified squamous epithelium of oral, crop, and esophageal mucosa. Moreover, it is possible to observe epithelial hyperplasia, necrosis, and infiltration of macrophages, lymphocytes, plasma cells, and heterophils [5,16,19].

4. Diagnosis

4.1. Microscopic examination

Due to the distinct and recognizable clinical signs associated with candidiasis, diagnosis can be reliably achieved through various methods. One such approach involves the examination of *Candida* spp. in samples obtained from feces, crop contents, skin, or regurgitated material. This assessment is conducted using staining techniques, such as Gram stain, Romanowsky-type stain, or new methylene blue stain (Figure 3)[17]. Upon direct observation, various forms of *Candida* spp. can be identified. These include thick-walled chlamydospores, ovoid or round budding yeast cells, hyphae, or pseudohyphae[6].

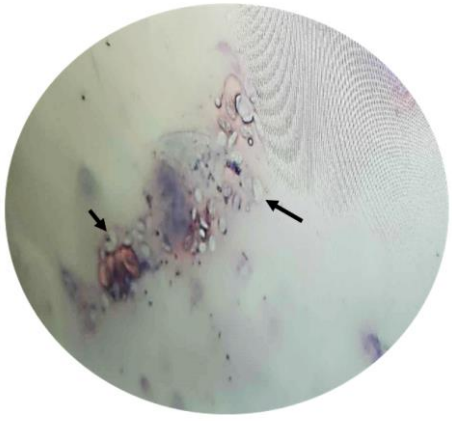

Figure 3. Cytology from plaques on the oral cavity of a *Buteo buteo* stained with Diff Quick showing *Candida* spp (100x, Source: Andreia Garcês).

Figure 4. *Candida lusitanea* isolated from *Milvus milvus* cultivated in CHROMID® *Candida*/Sabouraud Gentamicin Chloramphenicol 2 Agar. It is observed blue, dome-shaped, and glistening colonies with 2-3 mm of diameter and dome-shaped glistening colonies with 2-3 mm diameter (Source: Andreia Garcês).

4.2. Culture and isolation

The standard media used to cultivate *Candida* spp. is solid Sabouraud dextrose Agar [6]. There are other mediums, such as CHROMID® *Candida*/Sabouraud Gentamicin Chloramphenicol 2 Agar (Biómerieux, France), that are Chromogenic mediums and allow the selective isolation of yeast and the direct identification of some *Candida* spp. since they have a similar appearance of colonies on growth media[16]. The agar should be incubated at 37°C for 2 to 5 days in anaerobic conditions [5,6,17]. After incubation, it is possible to observe white, dome-shaped, and glistening colonies with 2-3 mm of diameter[17] (Figure 4).

Wet mount preparations are created from culture colonies or mucous membranes. These preparations can be directly examined or fixed and subsequently stained using stains such as Gram stain, Wright's stain, or Giemsa stain. When grown on suitable growth media, *Candida* spp. typically appear as oval budding yeast cells (Figure 5)[17]. On the other hand, within bird tissues, *Candida* spp. exhibit polymorphism, giving rise to structures like pseudohyphae or hyphae [17].

Candida albicans can be identified by the formation of chlamydospores on certain media such as Corn Meal Agar

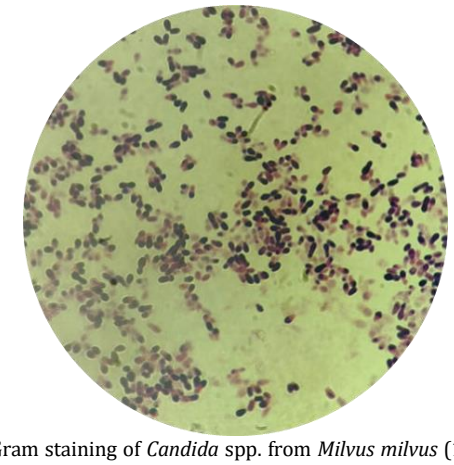

Figure 5. Gram staining of *Candida* spp. from *Milvus milvus* (100x, Source: Andreia Garcês).

and Chlamydospore Agar. When incubated in serum at 37°C for 2 hours, they form germ tubes [17,20]. The species can be identified using API or VITEK® system (Biomérieux, France)[5].

4.3. Molecular diagnoses

The serological diagnosis, including flocculation tests, neutralization tests, hemagglutinin-inhibition tests, enzyme-linked immunosorbent assays (ELISAs), and chemiluminescence immunoassays, is a commonly employed method for detecting systemic Candidiasis. It involves immune diffusion for the detection of antigens, which is favored due to its heightened specificity and sensitivity[6]. Another molecular approach utilized is the polymerase chain reaction (PCR), which also finds application in Candidiasis diagnosis[5].

6. Prevention, treatment, and control

5.1. Prevention and control

Good sanitary conditions of the infrastructure or installations, along with the elimination of any predisposing factors, are enough for the prevention of candidiasis[6]. When the infected animal is identified, it should be isolated from other animals since they are a potential source of infection[5,10].

5.2. Treatment

Treatment for candidiasis involves the administration of antifungal agents. In the case of fertile eggs, a preventive measure involves dipping them in an iodine solution to hinder the transmission of the pathogen from infected parent birds to newly hatched chicks via the eggshell[6]. In neonates that present crop stasis, it's crucial to empty the crop and feed smaller amounts until the crop stasis resolves. The use of Metoclopramide can aid in promoting crop motility and preventing regurgitation in such cases[6,16]. Administration of Metoclopramide may help crop motility and prevent regurgitation in stage[5,6,16]. Nystatin (300,000 IU/kg, orally, twise a day for 5 days or at a dose of 10 mg/kg q12h for 14 days) is the most commonly used drug for treatment due to its low cost and low toxicity[21,22]. Other compounds can be used when there is resistance to nystatin fluconazole (20 mg/kg, orally, every 48 hours), parconazole, ketoconazole, Diflucan, Nizoraand, gentian violet but can present some toxic effects in some animals[5]. Although yeast species like *Candida* generally do not easily develop resistance to antifungals, it is advisable to conduct antifungal sensitivity tests to determine the presence of resistance, especially as certain *Candida* species are beginning to acquire resistance[23].

6. Conclusion

Candidiasis is an important disease in birds, both wild and domestic, that sometimes is overlooked but can have hazardous effects. While the likelihood of zoonotic transmission is low, it remains a point of consideration. Continuously, new species and strains of pathogens are being identified, underscoring the necessity of diagnose and management of this disease. The present review serves as a concise resource to aid in recognizing and treating candidiasis. In the future, the potential rise in antifungal resistance, especially among domestic birds, is a cause for concern due to the potential for significant economic repercussions. Thus, it becomes imperative to include *Candida* spp. as a possible diagnosis when confronted with corresponding symptoms. Implementing effective treatment strategies is crucial for minimizing the prevalence of resistance. Prevention emerges as the most effective means of disease control.

Declarations

Competing interests

The authors declare that they have no competing interests.

Author's contribution

Andreia Garcês developed the methodology collaboratively, ensuring a comprehensive approach to the investigation. Andreia Garcês also carried out the investigation, collectively contributing to the data collection and analysis process. Andreia Garcês performed the writing of the original draft of the manuscript.

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Ethical considerations

The ethical issues, including consent to publish, misconduct, fabrication of data, and redundancy, have been checked by the authors.

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